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Case Report

A severe monkeypox infection in a patient with an advanced HIV infection treated with tecovirimat: clinical and virological outcome

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ABSTRACT

A patient aged 28 years who is immunocompromised and living with HIV/AIDS became infected with the monkeypox virus (MPXV). His clinical condition deteriorated for 37 days, with fever, skin lesions, and diarrhea before going to the infectious diseases department, where his severe, protracted infection was treated with tecovirimat for 14 days. His condition rapidly improved, and the skin lesions decreased, as did the MPXV loads, with no adverse events. This case indicates that tecovirimat might be effective for treating patients who are immunocompromised and are infected with MPXV.

Introduction

The worldwide outbreak of monkeypox (MPX) that began in May 2022 was declared a public health emergency of international concern by the World Health Organization on July 23, 2022 (World Health Organization, 2022). Most of the more than 52,000 cases identified by August 31, 2022 (Centers for Disease Control and Prevention, 2022a) had mild, self-limited symptoms that require only supportive care (Thornhill *et al.*, 2022). However, severe forms requiring specific antiviral treatment can occur, particularly in patients who are immunocompromised, such as those with an advanced HIV infection (Boesecke *et al.*, 2022; de Sousa *et al.*, 2022a). The VP37 inhibitor, tecovirimat, was approved by the Food and Drug Administration in 2018 for treating smallpox (Food and Drug Administration, 2018) and by the European Medicines Agency in 2022 for treating smallpox, cowpox, and MPX (European Medicines Agency, 2022). Its effectiveness and safety for treating MPX in humans, particularly in patients who are immunocompromised, have not been assessed. We report here the clinical and virological outcome of a case of disseminated, protracted MPX infection in a patient who is severely immunocompromised with advanced HIV infection, treated with tecovirimat.

Case description

A man aged 28 years having sex with men, with no past medical history, developed a fever with a profuse pustular rash and asthenia on July 15, 2022. An MPX infection was diagnosed on August 1, 2022, when the virus was detected by a nucleic acid amplification test on pustule, saliva, and nasopharyngeal samples (Figure 1). He reported a single sexual partner and contact with a patient infected with MPX in Spain in early July 2022. He had fever and inguinal lymphadenopathies, without severe anorectal pain, soft-tissue superinfection, or signs of myocarditis, encephalitis, and respiratory or digestive involvement. He was not screened for sexually transmitted infections (STIs) at that time and was asked to isolate himself at home with supportive care only. His fever persisted with moderate shivers, his skin lesions worsened, and abundant watery diarrhea (6/day) began, while his general condition deteriorated. He was admitted to the hospital on August 24, with a temperature of 40.5°C and a pulse of 140/min but no sign of sepsis. Examination revealed about 25 painful, inflammatory crusted lesions, with a diameter of 2-3 cm scattered over his face, scalp, trunk, limbs, and anal margins, associated with scalp cellulitis

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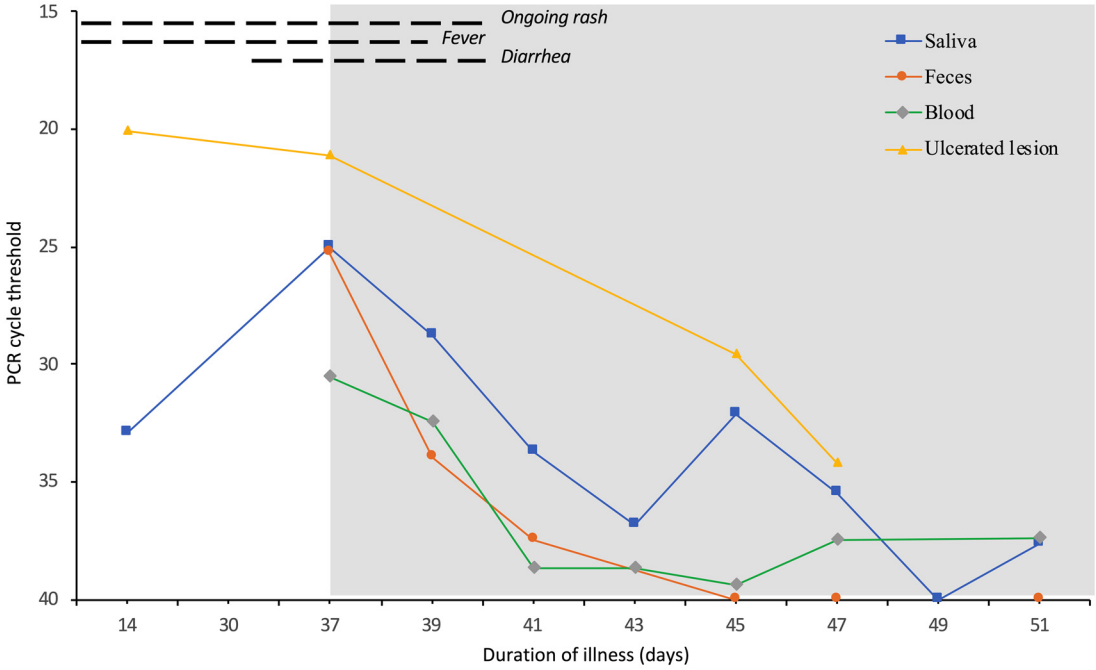

Figure 1. Clinical and virological timelines. Ct denotes the number of PCR cycles required to detect monkeypox virus DNA. A high Ct indicates a low virus load. We consider the virus to be undetectable if the threshold is above Ct: 40. The durations of rash, fever and diarrhea are indicated by dashed lines. The gray background indicates days on tecovirimat with a first dose administrated on day 37 of illness. Ct, cycle threshold; PCR, polymerase chain reaction.

(Figure S1). Blood cell counts, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and troponin levels were all normal, as was the electrocardiogram and whole-body computed tomography. Blood c-reactive protein was elevated (159 mg/l, N <5 mg/l). Diagnostic workup revealed an advanced HIV-1/AIDS infection with a plasma viral load of 5.8 $\log_{10}$ copies/ml and a cluster of differentiation 4^+ T cell count of 63/μl (5%). Screening for opportunistic infections; viral hepatitis A, B, and C; gonorrhea; chlamydiosis; and in stools, enteropathogens and protozoal infections were negative, except for latent syphilis. The MPX virus (MPXV) DNA was still detected in skin lesions (cycle threshold: 21), and saliva (cycle threshold: 25). Whole blood and stool samples also contained MPXV DNA, and his scalp lesions had superinfections with *Klebsiella aerogenes* and *Staphylococcus lugdunensis*. Intravenous antibacterial therapy with amoxicillin-clavulanate promptly replaced by oral cotrimoxazole for 7 days was initiated on August 24. Oral tecovirimat 600 mg twice daily for 14 days was initiated on August 25. The fever subsided from August 27, and the diarrhea resolved on August 28; furthermore, the disseminated skin lesions improved and became less inflamed. His skin lesions had almost completely healed, with full desquamation after 14 days on tecovirimat (Figure S1), and his MPXV load was reduced, although with inconsistency regarding saliva (Figure 1). His feces became MPXV DNA-negative on day 9 and remained so. HIV antiretroviral therapy (bictegravir, tenofovir alafenamide, and emtricitabine) was started on August 31, and the syphilis infection was treated with three benzathine benzylpenicillin weekly injections. The only adverse effect was a transient rise in ALT (acme 97 IU/l) and AST activities (acme 86 IU/l) from August 27 to September 2. The patient was discharged on September 8.

Discussion

The effectiveness of tecovirimat for treating MPX is based on placebo-controlled studies on macaques. Tecovirimat reduced the virus load and skin lesions and improved survival (Russo *et al.*, 2018). A recent retrospective study and an uncontrolled study on 25 patients with MPX found that tecovirimat reduced the time they were symptomatic and viremic, but the drug's efficacy has never been proved in clinical trials (Adler *et al.*, 2022; Desai *et al.*, 2022). Our case does not directly establish the effectiveness of tecovirimat. Nevertheless, we believe that the improvement in the skin lesions, which lasted for more than a month, the prompt resolution of diarrhea that could be attributed to MPX (Bragazzi *et al.*, 2022), and the progressive decrease in the MPXV load all suggest that tecovirimat is an effective treatment. This patient will be followed-up virologically to detect any relapse and emergence of resistance to tecovirimat (Duraffour *et al.*, 2015). The tecovirimat safety profile was excellent in the current case with no adverse events. The transient rise in ALT and AST activities was possibly related to the antibacterial treatment.

Tecovirimat is currently indicated for patients developing severe MPX and for patients at high risk of severe disease (patients who are immunocompromised or pediatric patients and pregnant women) (Centers for Disease Control and Prevention, 2022b). Men having sex with men living with HIV/AIDS are over-represented in the population infected in the current MPX outbreak (Thornhill *et al.*, 2022). Patients with an advanced HIV infection and related immunodepression are of particular concern; although, other immunocompromised subjects may also be at risk of severe, protracted disease if MPX spreads to the general population. Patients with newly diagnosed HIV infection at the time of MPX diagnosis should initiate antiretroviral therapy as soon as possible (O'Shea *et al.*, 2022) but the risk of subsequent immune reconstitution inflammatory syndrome needs to be determined. This risk might be mitigated by reducing the MPXV load with tecovirimat.

This case report highlights two points. First, bacterial cellulitis contributed to the systemic symptoms of our patient. Patients should be checked for bacterial soft-tissue superinfections because they often complicate MPX infections (de Sousa *et al.*, 2022b; Thornhill *et al.*, 2022). Second, although the detection of MPXV in seminal fluid samples is not definitive evidence of infectivity, human-to-human transmission frequently occurs after recent close sexual contact (Thornhill *et al.*, 2022). MPX should therefore be

considered as a new possible STI, and patients diagnosed with MPX should be routinely tested for HIV and other STIs (Brundu *et al.*, 2022).

This case indicates that tecovirimat might be effective for reducing the prolonged excretion of MPXV in a patient who is immunocompromised and living with HIV. However, large trials are still required to determine whether tecovirimat is a safe, effective treatment for MPX, particularly for patients who are immunocompromised.

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Ethical approval

Written informed consent was obtained from the patient.

Author contributions

The authors confirm contribution to the paper as follows: study conception and design: Clément Viguier, Tristan de Kermel, Guillaume Martin-Blondel, Jean-Michel Mansuy, Xavier Boumaza; data collection: Clément Viguier, Tristan de Kermel, Guillaume Martin-Blondel, Jean-Michel Mansuy; analysis and interpretation of results: Clément Viguier, Tristan de Kermel, Guillaume Martin-Blondel, Jean-Michel Mansuy, Christophe Pasquier; draft manuscript preparation: Clément Viguier, Tristan de Kermel, Guillaume Martin-Blondel. All authors reviewed the results and approved the final version of the manuscript.

Declaration of competing interest

The authors have no competing interests to declare.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2022.10.031.

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